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CHAKRABARTI, ARUN K

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1634	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/892,485	Ishihara
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 15, 2002*.

2a) ☒ This action is **FINAL.** 2b) ☐ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *1-4, 6-10, 15-20, and 24-28* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *1-4, 6-10, 15-20, and 24-28* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Specification

1. Claim 5 has been canceled without prejudice towards further prosecution. Claims 1-4, 6-10, and 14-20 have been amended. New claims 24-28 have been added.

Claim Rejections - 35 USC § 102

2. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

3. Claims 1-4 are rejected under 35 U.S.C. 102 (e) as being anticipated by Lonial et al. (U.S. Patent 6,001,560) (December 14, 1999).

Lonial et al teach a method of detecting an endocrine disrupting action of a test substance (Abstract), comprising:

a) culturing a cell having a sensitivity to an endocrine hormone in a first culture system in which endocrine hormone and the test substance are present (Claim 12 and column 10, line 65 to column 12, line 16);

b) determining the presence or absence of an endocrine disrupting action of the test substance by comparing a first gene expression pattern obtained from the cell of the first culture

system with a second gene expression pattern expressed by a cell having a sensitivity to the endocrine hormone (Claim 12 and column 10, line 65 to column 12, line 16 and Figure 3).

Lonial et al inherently teach a method comprising a second, third and fourth culture system in which presence and absence of endocrine hormone and test substances are modulated (Claim 12 and column 10, line 65 to column 12, line 16 and Figure 3).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

5. Claims 7, 9, and 15-17 are rejected under 35 U.S.C. 103 (a) over Lonial et al. (U.S. Patent 6,001,560) (December 14, 1999) in view of Gillies et al. (U.S. Patent 4,663,281) (May 5, 1987).

Lonial et al teach a method of claims 1-4 as described above.

Lonial et al do not teach a method, wherein comparison of the gene expression patterns are made by comparing bands obtained by subjecting a gene group contained in each of gene expression patterns to electrophoretic separation.

Gillies et al teach a method, wherein comparison of the gene expression patterns are made by comparing bands obtained by subjecting a gene group contained in each of gene expression patterns to electrophoretic separation (Figures 2, 7, and 8).

Lonial et al do not teach a method, wherein comparison of the gene expression patterns are made by hybridizing gene groups, and subtracting unhybridized genes.

Gillies et al teach a method, wherein comparison of the gene expression patterns are made by hybridizing gene groups, and subtracting unhybridized genes (Figures 7-8).

Lonial et al do not teach a method, wherein glycoprotein is expressed in cells.

Gillies et al teach a method, wherein glycoprotein is expressed in cells (Column 5, lines 30-37).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein glycoprotein is expressed in cells and wherein comparison of the gene expression patterns are made by comparing bands obtained by subjecting a gene group contained in each of gene expression patterns to electrophoretic separation of Gillies et al in the method of Lonial et al, since Gillies et al states, "More specifically, the invention relates to a method of exploiting the genetic mechanism of

certain types of eukaryotic cells to produce relatively large quantities of a protein of interest or its precursor (Column 1, lines 11-15)" Moreover, Lonial et al provide further motivation as Lonial et al state, "The search for such agonists and antagonists would be facilitated by the development of a fast and effective in vitro screening system (Column 2, lines 29-31)". By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the method wherein glycoprotein is expressed in cells and wherein comparison of the gene expression patterns are made by comparing bands obtained by subjecting a gene group contained in each of gene expression patterns to electrophoretic separation of Gillies et al in the method of Lonial et al. in order to improve the process for detecting an endocrine disrupting action of a test substance and in order to achieve the express advantages, as noted by Gillies et al, of an invention which relates to a method of exploiting the genetic mechanism of certain types of eukaryotic cells to produce relatively large quantities of a protein of interest or its precursor and also in order to achieve the express advantages, as noted by Lonial et al, which would facilitate the search for hormone agonists and antagonists by the development of a fast and effective in vitro screening system.

6. Claims 8 and 10 are rejected under 35 U.S.C. 103 (a) over Lonial et al. (U.S. Patent 6,001,560) (December 14, 1999) in view of Pearson et al. (U.S. Patent 5,916,779) (June 29, 1999).

Lonial et al teach a method of claims 1-4 as described above.

Lonial et al do not teach a method, wherein RNA is recovered and subjected to RT PCR to detect a band specific to gene expression pattern.

Pearson et al teach a method, wherein RNA is recovered and subjected to RT PCR to detect a band specific to gene expression pattern (Abstract, Claim 1 and Figure 1 and Column 2, lines 13-56).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein RNA is recovered and subjected to RT PCR to detect a band specific to gene expression pattern of Pearson et al in the method of Lonial et al, since Pearson et al states, "Amplification of RNA and DNA targets is often desirable for diagnostic application of amplification technologies, as this gives the greatest number of amplifiable targets per sample. , and as a result, the greatest diagnostic sensitivity. Amplification of RNA targets is also useful for diagnostic monitoring of RNA-related conditions such as certain viremias, up regulation of cancer genes, etc. Amplification of RNA targets is referred to as "reverse transcription amplification", the best known method being reverse transcription PCR.(Column 2, lines 17-26)". Moreover, Lonial et al provide further motivation as Lonial et al state, "The search for such agonists and antagonists would be facilitated by the development of a fast and effective in vitro screening system (Column 2, lines 29-31)". By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the method wherein RNA is recovered and subjected to RT PCR to detect a band specific to gene expression pattern of Pearson et al in the method of Lonial et al. in order to

improve the process for detecting an endocrine disrupting action of a test substance and in order to achieve the express advantages, as noted by Pearson et al, of an invention which provides amplification of RNA targets by the best known method reverse transcription PCR useful for diagnostic monitoring of RNA-related conditions such as certain viremias, up regulation of cancer genes, etc. and also in order to achieve the express advantages, as noted by Lonial et al, which would facilitate the search for hormone agonists and antagonists by the development of a fast and effective in vitro screening system.

7. Claim 6 is rejected under 35 U.S.C. 103 (a) over Lonial et al. (U.S. Patent 6,001,560) (December 14, 1999) in view of Comoglio et al. (U.S. Patent 6,030,949) (February 29, 2000) further in view of Cubicciotti (U.S. Patent 6,287,765 B1) (September 11, 2001).

Lonial et al teach a method of claims 1-4 as described above.

Lonial et al do not teach a method, wherein cell is Neuro2a.

Comoglio et al. teach a method, wherein cell is Neuro2a (Examples 2 and 3).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute a method, wherein cell is Neuro2a of Comoglio et al in the method of Lonial et al, since Comoglio et al states, "The invention refers to transduced cells for use in the therapy of the above mentioned pathologies (Column 2, lines 6-8)". Moreover, Lonial et al provide further motivation as Lonial et al state, "The search for such agonists and antagonists would be facilitated by the development of a fast and effective in vitro screening system (Column 2, lines 29-31)". By employing scientific reasoning, an ordinary practitioner

would have been motivated to combine and substitute the method wherein glycoprotein is expressed in cells and wherein comparison of the gene expression patterns are made by comparing bands obtained by subjecting a gene group contained in each of gene expression patterns to electrophoretic separation of Gillies et al in the method of Lonial et al. in order to improve the process for detecting an endocrine disrupting action of a test substance and in order to achieve the express advantages, as noted by Comoglio et al, of an invention which refers to transduced cells for use in the therapy of certain neurodegenerative pathologies and also in order to achieve the express advantages, as noted by Lonial et al, which would facilitate the search for hormone agonists and antagonists by the development of a fast and effective in vitro screening system.

Lonial et al. in view of Comoglio et al do not teach a method, wherein endocrine hormone is triiodothyronine.

Cubicciotti teaches a method, wherein endocrine hormone is triiodothyronine (Column 182, lines 18-46).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute a method, wherein endocrine hormone is triiodothyronine of Cubicciotti in the method of Lonial et al. in view of Comoglio et al., since Cubicciotti states, "Examples of analytes for which such a complex is useful include, but are not limited to, hormones such as thyroxine and triiodothyronine (Column 182, lines 28-30)". Moreover, Lonial et al provide further motivation as Lonial et al state, "The search for such agonists and antagonists would be facilitated by the development of a fast and effective in vitro

screening system (Column 2, lines 29-31)". By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the method wherein endocrine hormone is triiodothyronine of Cubicciotti in the method of Lonial et al. in view of Comoglio et al. in order to improve the process for detecting an endocrine disrupting action of a test substance and in order to achieve the express advantages, as noted by Cubicciotti, of triiodothyronine which refers to examples of equivalent useful analyte complex and also in order to achieve the express advantages, as noted by Lonial et al, which would facilitate the search for hormone agonists and antagonists by the development of a fast and effective in vitro screening system.

8. Claims 18-19 are rejected under 35 U.S.C. 103 (a) over Lonial et al. (U.S. Patent 6,001,560) (December 14, 1999) in view of Gillies et al. (U.S. Patent 4,663,281) (May 5, 1987) further in view of Comoglio et al. (U.S. Patent 6,030,949) (February 29, 2000) further in view of Cubicciotti (U.S. Patent 6,287,765 B1) (September 11, 2001)..

Lonial et al. in view of Gillies et al teach the method of claims 1-4, 7, 9, and 15-17 as described above.

Lonial et al. in view of Gillies et al do not teach a method, wherein cell is Neuro2a.

Comoglio et al. teach a method, wherein cell is Neuro2a (Examples 2 and 3).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute a method, wherein cell is Neuro2a of Comoglio et al in the method of Lonial et al in view of Gillies et al, since Comoglio et al states, "The invention refers to transduced cells for use in the therapy of the above mentioned pathologies

(Column 2, lines 6-8)". Moreover, Lonial et al provide further motivation as Lonial et al state, "The search for such agonists and antagonists would be facilitated by the development of a fast and effective in vitro screening system (Column 2, lines 29-31)". By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the method wherein glycoprotein is expressed in cells and wherein comparison of the gene expression patterns are made by comparing bands obtained by subjecting a gene group contained in each of gene expression patterns to electrophoretic separation of Gillies et al in the method of Lonial et al. in view of Gillies et al in order to improve the process for detecting an endocrine disrupting action of a test substance and in order to achieve the express advantages, as noted by Comoglio et al, of an invention which refers to transduced cells for use in the therapy of certain neurodegenerative pathologies and also in order to achieve the express advantages, as noted by Lonial et al, which would facilitate the search for hormone agonists and antagonists by the development of a fast and effective in vitro screening system.

Lonial et al. in view of Gillies et al. further in view of Comoglio et al. do not teach a method, wherein endocrine hormone is triiodothyronine.

Cubicciotti teaches a method, wherein endocrine hormone is triiodothyronine (Column 182, lines 18-46).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute a method, wherein endocrine hormone is triiodothyronine of Cubicciotti in the method of Lonial et al. in view of Gillies et al. further in

view of Comoglio et al., since Cubicciotti states, "Examples of analytes for which such a complex is useful include, but are not limited to, hormones such as thyroxine and triiodothyronine (Column 182, lines 28-30)". Moreover, Lonial et al provide further motivation as Lonial et al state, "The search for such agonists and antagonists would be facilitated by the development of a fast and effective in vitro screening system (Column 2, lines 29-31)". By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the method wherein endocrine hormone is triiodothyronine of Cubicciotti in the method of Lonial et al. in view of Gillies et al. further in view of Comoglio et al., in order to improve the process for detecting an endocrine disrupting action of a test substance and in order to achieve the express advantages, as noted by Cubicciotti, of triiodothyronine which refers to examples of equivalent useful analyte complex and also in order to achieve the express advantages, as noted by Lonial et al, which would facilitate the search for hormone agonists and antagonists by the development of a fast and effective in vitro screening system.

9. Claim 20 is rejected under 35 U.S.C. 103 (a) over Lonial et al. (U.S. Patent 6,001,560) (December 14, 1999) in view of Gillies et al. (U.S. Patent 4,663,281) (May 5, 1987) further in view of Makari (U.S. Patent 4,752,471).

Lonial et al. in view of Gillies et al teach the method of claims 1-4, 7, 9, and 15-17 as described above including the electrophoresis.

Lonial et al. in view of Gillies et al do not teach a method, wherein protein is recovered from the glycoprotein by cutting off the polysaccharide chain.

Makari teaches a method, wherein protein is recovered from the glycoprotein by cutting off the polysaccharide chain (Claim 5).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein protein is recovered from the glycoprotein by cutting off the polysaccharide chain. of Makari in the method of Lonial et al in view of Gillies et al., since Makari states, "The present invention relates to cancer detection preparations, their administrations and their methods of manufacture (Column 1, lines 28-30)." Moreover, Lonial et al provide further motivation as Lonial et al state, "The search for such agonists and antagonists would be facilitated by the development of a fast and effective in vitro screening system (Column 2, lines 29-31)". By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the method wherein protein is recovered from the glycoprotein by cutting off the polysaccharide chain. of Makari in the method of Lonial et al. in view of Gillies et al in order to improve the process for detecting an endocrine disrupting action of a test substance and in order to achieve the express advantages, as noted by Makari, of an invention which relates to cancer detection preparations, their administrations and their methods of manufacture and also in order to achieve the express advantages, as noted by Lonial et al, which would facilitate the search for hormone agonists and antagonists by the development of a fast and effective in vitro screening system.

10. Claim 24 is rejected under 35 U.S.C. 103 (a) over Lonial et al. (U.S. Patent 6,001,560) (December 14, 1999) in view of Soto et al. (U.S. Patent 5,135,849) (August 4, 1992) further in view of Makari (U.S. Patent 4,752,471).

Lonial et al. teach the method of claims 1-4 as described above.

Lonial et al. do not teach a method, wherein the endocrine hormone is selected from a male hormone.

Soto et al. teach a method, wherein the endocrine hormone is selected from a male hormone.(Abstract and Claims 1-12, and Column 11, line 53 to Column 28, line 13).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein the endocrine hormone is selected from a male hormone of Soto et al. in the method of Lonial et al., since Soto et al. states, "The methodology is rapid, reproducible, and accurate, and provides the major advantage of being able to test large numbers of unevaluated substances for their androgen agonistic and/or antagonistic properties as primary properties or secondary side-effects (Abstract, last sentence)." Moreover, Lonial et al provide further motivation as Lonial et al state, "The search for such agonists and antagonists would be facilitated by the development of a fast and effective in vitro screening system (Column 2, lines 29-31)". By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the method, wherein the endocrine hormone is selected from a male hormone of Soto et al. in the method of Lonial et al. in order to improve the process for detecting an endocrine disrupting action of a test substance and

in order to achieve the express advantages, as noted by Soto et al., of an invention which is rapid, reproducible, and accurate, and provides the major advantage of being able to test large numbers of unevaluated substances for their androgen agonistic and/or antagonistic properties as primary properties or secondary side-effects.

Lonial et al. in view of Soto et al. do not teach a method, wherein protein is recovered from the glycoprotein by cutting off the polysaccharide chain.

Makari teaches a method, wherein protein is recovered from the glycoprotein by cutting off the polysaccharide chain (Claim 5).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein protein is recovered from the glycoprotein by cutting off the polysaccharide chain. of Makari in the method of Lonial et al in view of Soto et al., since Makari states, "The present invention relates to cancer detection preparations, their administrations and their methods of manufacture (Column 1, lines 28-30)." Moreover, Lonial et al provide further motivation as Lonial et al state, "The search for such agonists and antagonists would be facilitated by the development of a fast and effective in vitro screening system (Column 2, lines 29-31)". By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the method wherein protein is recovered from the glycoprotein by cutting off the polysaccharide chain. of Makari in the method of Lonial et al. in view of Soto et al. in order to improve the process for detecting an endocrine disrupting action of a test substance and in order to achieve the express advantages, as noted by

Makari, of an invention which relates to cancer detection preparations, their administrations and their methods of manufacture and also in order to achieve the express advantages, as noted by Lonial et al and Soto et al., which would facilitate the search for hormone agonists and antagonists by the development of a fast and effective in vitro screening system.

11. Claim 25 is rejected under 35 U.S.C. 103 (a) over Lonial et al. (U.S. Patent 6,001,560) (December 14, 1999) in view of Soto et al. (U.S. Patent 5,135,849) (August 4, 1992) further in view of Makari (U.S. Patent 4,752,471) further in view of Comoglio et al. (U.S. Patent 6,030,949) (February 29, 2000).

Lonial et al. in view of Soto et al. further in view of Makari teach the method of claim 24 as described above.

Lonial et al. in view of Soto et al. further in view of Makari do not teach the method wherein cell is Neuro2a.

Comoglio et al. teach a method, wherein cell is Neuro2a (Examples 2 and 3).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute a method, wherein cell is Neuro2a of Comoglio et al in the method of Lonial et al. in view of Soto et al. further in view of Makari, since Comoglio et al states, "The invention refers to transduced cells for use in the therapy of the above mentioned pathologies (Column 2, lines 6-8)". Moreover, Lonial et al provide further motivation as Lonial et al state, "The search for such agonists and antagonists would be facilitated by the development of a fast and effective in vitro screening system (Column 2, lines 29-31)". By employing scientific

reasoning, an ordinary practitioner would have been motivated to combine and substitute the method wherein cell is Neuro2a of Comoglio et al in the method of Lonial et al. in view of Soto et al. further in view of Makari in order to improve the process for detecting an endocrine disrupting action of a test substance and in order to achieve the express advantages, as noted by Comoglio et al, of an invention which refers to transduced cells for use in the therapy of certain neurodegenerative pathologies and also in order to achieve the express advantages, as noted by Lonial et al, which would facilitate the search for hormone agonists and antagonists by the development of a fast and effective in vitro screening system.

12. Claims 26 and 28 are rejected under 35 U.S.C. 103 (a) over Lonial et al. (U.S. Patent 6,001,560) (December 14, 1999) in view of Soto et al. (U.S. Patent 5,135,849) (August 4, 1992) further in view of Makari (U.S. Patent 4,752,471) further in view of Gillies et al. (U.S. Patent 4,663,281) (May 5, 1987).

Lonial et al. in view of Soto et al. further in view of Makari teach the method of claim 24 as described above.

Lonial et al. in view of Soto et al. further in view of Makari do not teach the method, wherein comparison of the gene expression patterns are made by comparing bands obtained by subjecting a gene group contained in each of gene expression patterns to electrophoretic separation.

Gillies et al teach a method, wherein comparison of the gene expression patterns are made by comparing bands obtained by subjecting a gene group contained in each of gene expression patterns to electrophoretic separation (Figures 2, 7, and 8).

Lonial et al in view of Soto et al. further in view of Makari do not teach a method, wherein comparison of the gene expression patterns are made by hybridizing gene groups, and subtracting unhybridized genes.

Gillies et al teach a method, wherein comparison of the gene expression patterns are made by hybridizing gene groups, and subtracting unhybridized genes (Figures 7-8).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein comparison of the gene expression patterns are made by comparing bands obtained by subjecting a gene group contained in each of gene expression patterns to electrophoretic separation of Gillies et al in the method of Lonial et al in view of Soto et al. further in view of Makari , since Gillies et al states, "More specifically, the invention relates to a method of exploiting the genetic mechanism of certain types of eukaryotic cells to produce relatively large quantities of a protein of interest or its precursor (Column 1, lines 11-15)" Moreover, Lonial et al provide further motivation as Lonial et al state, "The search for such agonists and antagonists would be facilitated by the development of a fast and effective in vitro screening system (Column 2, lines 29-31)". By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the method wherein glycoprotein is expressed in cells and wherein comparison of the gene expression

patterns are made by comparing bands obtained by subjecting a gene group contained in each of gene expression patterns to electrophoretic separation of Gillies et al in the method of Lonial et al. in view of Soto et al. further in view of Makari in order to improve the process for detecting an endocrine disrupting action of a test substance and in order to achieve the express advantages, as noted by Gillies et al, of an invention which relates to a method of exploiting the genetic mechanism of certain types of eukaryotic cells to produce relatively large quantities of a protein of interest or its precursor and also in order to achieve the express advantages, as noted by Lonial et al, which would facilitate the search for hormone agonists and antagonists by the development of a fast and effective in vitro screening system.

13. Claim 27 is rejected under 35 U.S.C. 103 (a) over Lonial et al. (U.S. Patent 6,001,560) (December 14, 1999) in view of Soto et al. (U.S. Patent 5,135,849) (August 4, 1992) further in view of Makari (U.S. Patent 4,752,471) further in view of in view of Pearson et al. (U.S. Patent 5,916,779) (June 29, 1999).

Lonial et al in view of Soto et al. further in view of Makari further in view of teach a method of claim 24 as described above.

Lonial et al in view of Soto et al. further in view of Makari do not teach a method, wherein RNA is recovered and subjected to RT PCR to detect a band specific to gene expression pattern.

Pearson et al teach a method, wherein RNA is recovered and subjected to RT PCR to detect a band specific to gene expression pattern (Abstract, Claim 1 and Figure 1 and Column 2, lines 13-56).

It would have been *prima facie* obvious to one having ordinary skill in the art at the time the invention was made to combine and substitute the method, wherein RNA is recovered and subjected to RT PCR to detect a band specific to gene expression pattern of Pearson et al in the method of Lonial et al in view of Soto et al. further in view of Makari , since Pearson et al states, "Amplification of RNA and DNA targets is often desirable for diagnostic application of amplification technologies, as this gives the greatest number of amplifiable targets per sample. , and as a result, the greatest diagnostic sensitivity. Amplification of RNA targets is also useful for diagnostic monitoring of RNA-related conditions such as certain viremias, up regulation of cancer genes, etc. Amplification of RNA targets is referred to as "reverse transcription amplification", the best known method being reverse transcription PCR.(Column 2, lines 17-26)". Moreover, Lonial et al provide further motivation as Lonial et al state, "The search for such agonists and antagonists would be facilitated by the development of a fast and effective in vitro screening system (Column 2, lines 29-31)". By employing scientific reasoning, an ordinary practitioner would have been motivated to combine and substitute the method wherein RNA is recovered and subjected to RT PCR to detect a band specific to gene expression pattern of Pearson et al in the method of Lonial et al. in view of Soto et al. further in view of Makari in order to improve the process for detecting an endocrine disrupting action of a test substance and in order to achieve the

express advantages, as noted by Pearson et al, of an invention which provides amplification of RNA targets by the best known method reverse transcription PCR useful for diagnostic monitoring of RNA-related conditions such as certain viremias, up regulation of cancer genes, etc. and also in order to achieve the express advantages, as noted by Lonial et al, which would facilitate the search for hormone agonists and antagonists by the development of a fast and effective in vitro screening system.

Response to Amendment

14. In response to amendment, 112 (second paragraph) rejections have been withdrawn. However, all previous 102(e) and 103(a) rejections have been properly maintained. Four new 103(a) rejections have been included.

Response to Arguments

15. Applicant's arguments and declaration filed on August 15, 2002 have been fully considered but they are not persuasive.

Applicant argues to withdraw 102(e) rejection in view of the fact that Lonial reference does not teach the detection of endocrine disrupting action of a test substance. This argument is not persuasive. In response to applicant's arguments, the recitation of detection of endocrine disrupting action of a test substance has not been given patentable weight because the recitation occurs in the preamble. A preamble is generally not accorded any patentable weight where it

merely recites the purpose of a process or the intended use of a structure, and where the body of the claim does not depend on the preamble for completeness but, instead, the process steps or structural limitations are able to stand alone. See *In re Hirao*, 535 F.2d 67, 190 USPQ 15 (CCPA 1976) and *Kropa v. Robie*, 187 F.2d 150, 152, 88 USPQ 478, 481 (CCPA 1951). Applicant also argues that Lonial does not teach culturing a cell sensitive to an endocrine hormone in the presence of the endocrine hormone and test substance and comparing the gene expression patterns of cells exposed to the test substance and the cells not exposed to the test substance. This argument is not persuasive. Lonial clearly teaches culturing a cell sensitive to an endocrine hormone in the presence of the endocrine hormone and test substance and comparing the gene expression patterns of cells exposed to the test substance and the cells not exposed to the test substance (Claim 12 and column 10, line 65 to column 12, line 16). Applicant also argues that method of Lonial would be ineffective, if the cell lines which express growth hormone reporter gene were grown in the presence of growth hormone, as the level of secreted growth hormone protein from the reporter gene could not be accurately measured. This argument is not persuasive. Any ordinary practitioner can add any measured and known amount of growth hormone in the cell culture medium and measure the total amount of growth hormone in the culture after certain period of time. If the known amount of growth hormone is subtracted from the total amount, the level of secreted growth hormone protein from the reporter gene could be accurately measured.

In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on

combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicant also argues that there is no motivation to combine the references. This argument is not persuasive, especially in the presence pf strong motivation provided by Pearson et al since Pearson et al. states, "Amplification of RNA and DNA targets is often desirable for diagnostic application of amplification technologies, as this gives the greatest number of amplifiable targets per sample. , and as a result, the greatest diagnostic sensitivity. Amplification of RNA targets is also useful for diagnostic monitoring of RNA-related conditions such as certain viremias, up regulation of cancer genes, etc. Amplification of RNA targets is referred to as "reverse transcription amplification", the best known method being reverse transcription PCR.(Column 2, lines 17-26)". The same logic is applicable to other references as well.

Conclusion

16. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CAR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CAR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D., whose telephone number is (703) 306-5818. The examiner can normally be reached on 7:00 AM-4:30 PM from Monday to Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group analyst Chantae Dessau whose telephone number is (703) 605-1237.

Arun Chakrabarti,

Patent Examiner,

February 26, 2003

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